CASE REPORT

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Patient with FMF and Triple MEFV Gene Mutations

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ABSTRACT

Introduction: Familial Mediterranean fever (FMF) is the most common auto-inflammatory disease with monogenic (MEditerranean FeVer –MEFV- gene) inherited pattern. It mainly affects ethnic groups living along the eastern Mediterranean Sea: Turks, Sephardic Jews, Armenians, and Arabs [1]. Today FMF is not rare disease in other Mediterranean ethnicities, such as Greeks, Italians, and Iranians. **Case report:** Here we report a child with complex allele mutations E148Q/V726A/R761H, whilst, whose mother showed E148Q/V726A and his father had R761H/wt in analysis. The severity of the disease and genotype-phenotype correlation of patient showed no significant differences with his mother and other patients with the same two mutations, V726A/R761H, E148Q/V726A, and E148Q/ R761H. **Conclusion: T**his type of mutation is the first report of triple mutations in FMF patients with no specific phenotype correlation.
Key words: FMF, MEFV Gene, Triple mutations.

1. INTRODUCTION

Familial Mediterranean fever (FMF) is the most common auto-inflammatory disease with monogenic (MEditerranean FeVer –MEFV- gene) inherited pattern. It mainly affects ethnic groups living along the eastern Mediterranean Sea: Turks, Sephardic Jews, Armenians, and Arabs (1). Today FMF is not rare disease in other Mediterranean ethnicities, such as Greeks, Italians, and Iranians (2, 3). Several series of non-endemic areas have been reported recently (4).

It is characterized by short inflammatory episodes of polyserositis, and fever with irregular pattern (1). Amyloidosis "as the major cause of mortality "is the most significant complication of FMF, and may be prevented by colchicine (5).

The MEFV gene, associated with the disease is located on chromosome 16. This gene encodes a 781-amino-acid protein named pyrin (6). This protein appears to play a pivotal role in the regulation of both inflammation and apoptosis, and mutated pyrin lead to full-blown inflammation characterized by excessive Il-1ß secretion in FMF (6).

Mutations in the pyrin gene have been identified in the majority of FMF patients, include four conservative missense mutations (M694V, M680I, V726A , M694I), clustered in exon 10, which, together with mutation E148Q, in exon 2, account for the vast majority of MEFV gene abnormalities (7, 8).

Two mutations, hemo or heterozygotic, confirm suffering from FMF. A few patients with more than two mutations named "complex alleles mutations" have been reported–E148Q/P369S/M680I (G>C) and E148Q/P369S/M694V (9).

Some authors recommend especial mutations as a normal variation in specific area and people (8). It has been established that, the phenotypic variability of the disease is, at least, partly due to allelic heterogeneity in one side and environmental factors (10). On the other side, mutation M694V is associated with a severe phenotype and amyloidosis, and mutation V726A with a milder form of the disease (10). There is not clear data about genotype-phenotype correlation of patients with complex alleles' mutations.

2. CASE REPORT

Here we report a child with complex allele mutations E148Q/V726A/R761H, whilst, whose mother showed E148Q/V726A and his father had R761H/wt in analysis.

The severity of the disease and genotype-phenotype correlation of patient showed no significant differences with his mother and other patients with the same two mutations, V726A/R761H, E148Q/V726A, and E148Q/ R761H.

3. CONCLUSION

In our knowledge this type of mutation is the first report of triple mutations in FMF patients with no specific phenotype correlation.

CONFLICTS OF INTEREST: NONE DECLARED.

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